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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,435	04/30/2001	Lawrence Loomis	382280006	9074
26633	7590	11/28/2003	EXAMINER	
HELLER EHRMAN WHITE & MCAULIFFE LLP 1666 K STREET,NW SUITE 300 WASHINGTON, DC 20006			PRATS, FRANCISCO CHANDLER	
			ART UNIT	PAPER NUMBER
			1651	

DATE MAILED: 11/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/844,435	LOOMIS ET AL.	
	Examiner	Art Unit	
	Francisco C Prats	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-151 is/are pending in the application.
- 4a) Of the above claim(s) 1-26 and 38-151 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 27-37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 April 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
 a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The preliminary amendment filed April 30, 2001, has been received and entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claims 1-151 are pending.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § 120. As noted immediately above, the preliminary amendment filed April 30, 2001, claiming priority to application serial numbers 09/560,650 and 09/752,732 has been entered. However, serial number. Note that application serial number 09/560,650 claims priority as a continuation-in-part to application serial number 09/395,636, filed September 14, 1999, now U.S. Pat. No. 6,056,954, which is a continuation of application serial number 08/962,523, filed October 31, 1997, now U.S. Pat. No. 5,997,862.

The oath/declaration of inventorship is objected to because, as discussed immediately above, the priority claim to serial number 09/752,732 is improper since that application appears to be totally unrelated to the subject matter of this

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application, and does not have an inventor in common with 09/560,650 or this application. A new oath or declaration is required.

Election/Restrictions

Applicant's election of the group II invention, claims 27-37, in the paper filed October 29, 2003, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-26 and 38-151 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. As discussed immediately above, election was made **without** traverse in the paper filed October 29, 2003.

Claims 27-37 are examined on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 27 and 30-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gasson (EP 510 907) and Delisle (WO 96/07329) in view of Witte et al (FEMS Microbiology Letters 164:159-167 (1998)) and Stemmer (U.S. Pat. 5,605,793).

Each of Gasson (*Streptococcus*, see page 2, lines 31-35 and Delisle (*Haemophilus*, see page 12, lines 20-24) disclose the use of phage lysins for killing the claimed genera of bacteria. The artisan of ordinary skill, recognizing that the claimed species of *Streptococcus pneumonia* and *Haemophilus influenza* were well-known pathogenic bacteria, would therefore have been motivated by the disclosure of the cited references to have combined phage enzymes capable of lysing the claimed bacteria with any of the

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carriers disclosed in the references, or any carrier suitable for the lytic applications disclosed in those references.

The cited references also differ from the claims in that neither reference discloses the use of the chimeric or shuffled enzymes in the disclosed lytic applications. However, each of Witte and Stemmer demonstrates not only that chimeric and/or shuffled enzymes were known in the art, but also that chimeric and/or shuffled enzymes possessed advantages when compared to their non-recombinant counterparts. Specifically, Witte demonstrates that the E-L chimeric lytic enzymes disclosed therein possess the lytic activities of both of the parent enzymes, as opposed to single activities possessed by the parent enzyme molecules. See Table 1, on page 160. Moreover, note the extremely quick onset of lethality (1 minute) possessed by the chimeric protein made by the pRM1/3 plasmid, as compared to the parent enzymes (10 minutes and 20 minutes).

Further still, Stemmer demonstrates that enzyme shuffling results in enzymes having increased enzymatic activity. See e.g., column 9, lines 39-45. See also column 20, lines 12-15, discussing a 2 to 3 fold increase in beta lactamase activity resulting from shuffling. Thus, the artisan of ordinary skill, recognizing the advantages of using chimeric and/or shuffled enzymes, clearly would have been motivated to have used chimeric

and/or shuffled enzymes in the processes disclosed in Gasson and Delisle.

Claims 27-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gasson (EP 510 907) and Delisle (WO 96/07329) in view of Witte et al (FEMS Microbiology Letters 164:159-167 (1998)) and Stemmer (U.S. Pat. 5,605,793) as applied above to claims 27 and 30-37, and in further view of Diaz et al (Molecular Microbiology 19(4):667-681 (1996)).

As discussed above, Gasson and Delisle, when viewed in light of Witte and Stemmer, are considered to render claims 27 and 30-37 obvious. None of Gasson/Delisle/Witte/Stemmer discloses the use of a combination of holin and lysin enzymes, as recited in claims 28 and 29. However, Diaz clearly discloses that the combined activity of holins and lysins provides optimal lysis of bacterial cells, when compared to holins or lysins alone. See, e.g., page 671, right column. ("Simultaneous expression of *ejh* [i.e., holin] and *ejl* [i.e., lysin] (Fig. 4F,L) showed the strongest and fastest (already observed after 60 minutes of induction) impact on cell morphology") Thus, the artisan of ordinary skill clearly would have been motivated to have added a holin enzyme to the lysin enzymes of Gasson and Delisle, in order to ensure

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optimal lysis of target pathogenic bacteria. A holding of obviousness is therefore clearly required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 27 and 30-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of U.S. Patent Nos. 5,997,862, 6,017,528, 6,056,955 and 6,423,299, in view of Witte et al (FEMS Microbiology Letters 164:159-167 (1998)) and Stemmer (U.S. Pat. 5,605,793).

Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the cited patents contains claims either encompassing or directly reciting compositions comprising lytic enzymes and carriers for treatment of upper respiratory tract infections. Moreover, as discussed above, each of Witte and Stemmer demonstrates not only that chimeric and/or shuffled enzymes were known in the art, but also that chimeric and/or shuffled enzymes possessed advantages when compared to their non-recombinant counterparts.

Specifically, Witte demonstrates that the E-L chimeric lytic enzymes disclosed therein possess the lytic activities of both of the parent enzymes, as opposed to single activities possessed by the parent enzyme molecules. See Table 1, on page 160.

Moreover, note the extremely quick onset of lethality (1 minute) possessed by the chimeric protein made by the pRM1/3 plasmid, as compared to the parent enzymes (10 minutes and 20 minutes).

Further still, Stemmer demonstrates that enzyme shuffling results in enzymes having increased enzymatic activity. See e.g., column 9, lines 39-45. See also column 20, lines 12-15, discussing a 2 to 3 fold increase in beta lactamase activity resulting from shuffling. Thus, the artisan of ordinary skill, recognizing the advantages of using chimeric and/or shuffled enzymes, clearly would have been motivated to have used chimeric

and/or shuffled enzymes in the processes recited in the claims of the cited patents.

Claims 27-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of U.S. Patent Nos. 5,997,862, 6,017,528, 6,056,955 and 6,423,299, in view of Witte et al (FEMS Microbiology Letters 164:159-167 (1998)) and Stemmer (U.S. Pat. 5,605,793), as discussed above, and in further view of Diaz et al (Molecular Microbiology 19(4):667-681 (1996)).

As discussed above, the claims of applicant's previous patents, when viewed in light of Witte and Stemmer, render obvious the subject matter recited in claims 27 and 30-37. However, neither the cited patents nor Witte or Stemmer disclose the use of a combination of holin and lysin enzymes, as recited in claims 28 and 29. However, as discussed above, Diaz clearly discloses that the combined activity of holins and lysins provides optimal lysis of bacterial cells, when compared to holins or lysins alone. See, e.g., page 671, right column. ("Simultaneous expression of *ejh* [i.e., holin] and *ejl* [i.e., lysin] (Fig. 4F,L) showed the strongest and fastest (already observed after 60 minutes of induction) impact on cell morphology") Thus, the artisan of ordinary skill

clearly would have been motivated to have added a holin enzyme to the lysin enzyme compositions recited in the claims of applicant's previous patents, in order to ensure optimal lysis of target pathogenic bacteria. A terminal disclaimer is therefore clearly required.

Claims 27 and 30-37 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of copending Application Nos. 10/067,991 and 10/145,604 of in view of Witte et al (FEMS Microbiology Letters 164:159-167 (1998)) and Stemmer (U.S. Pat. 5,605,793).

Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the copending applications contains claims either encompassing or directly reciting compositions comprising lytic enzymes and carriers for treatment of upper respiratory tract infections. Moreover, as discussed above, each of Witte and Stemmer demonstrates not only that chimeric and/or shuffled enzymes were known in the art, but also that chimeric and/or shuffled enzymes possessed advantages when compared to their non-recombinant counterparts. Specifically, Witte demonstrates that the E-L chimeric lytic enzymes disclosed therein possess the lytic

activities of both of the parent enzymes, as opposed to single activities possessed by the parent enzyme molecules. See Table 1, on page 160. Moreover, note the extremely quick onset of lethality (1 minute) possessed by the chimeric protein made by the pRM1/3 plasmid, as compared to the parent enzymes (10 minutes and 20 minutes).

Further still, Stemmer demonstrates that enzyme shuffling results in enzymes having increased enzymatic activity. See e.g., column 9, lines 39-45. See also column 20, lines 12-15, discussing a 2 to 3 fold increase in beta lactamase activity resulting from shuffling. Thus, the artisan of ordinary skill, recognizing the advantages of using chimeric and/or shuffled enzymes, clearly would have been motivated to have used chimeric and/or shuffled enzymes in the processes recited in the claims of the copending applications.

This is a provisional obviousness-type double patenting rejection.

Claims 27-37 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of copending Application Nos. 10/067,991 and 10/145,604, in view of Witte et al (FEMS Microbiology Letters 164:159-167 (1998)) and Stemmer (U.S. Pat.

5,605,793), as discussed above, and in further view of Diaz et al (Molecular Microbiology 19(4):667-681 (1996)).

As discussed above, the claims of applicant's copending applications, when viewed in light of Witte and Stemmer, render obvious the subject matter recited in claims 27 and 30-37. However, neither the claims of the copending applications nor Witte or Stemmer disclose the use of a combination of holin and lysin enzymes, as recited in claims 28 and 29. However, as discussed above, Diaz clearly discloses that the combined activity of holins and lysins provides optimal lysis of bacterial cells, when compared to holins or lysins alone. See, e.g., page 671, right column. ("Simultaneous expression of *ejh* [i.e., holin] and *ejl* [i.e., lysin] (Fig. 4F,L) showed the strongest and fastest (already observed after 60 minutes of induction) impact on cell morphology") Thus, the artisan of ordinary skill clearly would have been motivated to have added a holin enzyme to the lysin enzyme compositions recited in the claims of applicant's copending applications, in order to ensure optimal lysis of target pathogenic bacteria. A terminal disclaimer is therefore clearly required.

This is a provisional obviousness-type double patenting rejection.

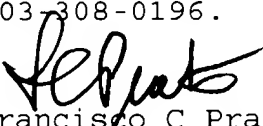
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No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C Prats whose telephone number is 703-308-3665. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G Wityshyn can be reached on 703-308-4743. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Francisco C Prats
Primary Examiner
Art Unit 1651

FCP